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Social Relations at Work and Incident Dementia: 29-Years' Follow-Up of the Copenhagen Male Study

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Objective: We investigated whether social relations at work were associated with incident dementia in old age. **Methods:** One thousand five hundred seventy-two occupationally active men from the Copenhagen Male Study Cohort were followed from 1986 to 2014. Participants underwent a clinical examination at baseline and answered questionnaires on whether they (1) had possibilities to be in contact with coworkers, (2) could get along with coworkers, and (3) were satisfied with supervisor. Poisson regression was used to estimate incidence rate ratios (IRR). **Results:** Two hundred forty five (15.6%) men were diagnosed with dementia during an average of 15.8 years of follow-up. After adjusting for potential confounders, limited contact with coworkers was associated with a higher risk of dementia (IRR = 2.49, 95% confidence interval [CI] 1.14 to 5.44), but the other two measures were not. **Conclusions:** Our data partially support that social relations at work are associated with incident dementia.

A growing body of evidence, summarized in a recent review of 19 studies,¹ suggests that having poor social relations is associated with an increased risk of dementia. More specifically, previous studies have reported a harmful effect of poor social network,^{2–5} weak social ties,^{3,5} lack of social engagement,^{1,4–6} infrequent social and leisure activity,^{1,5,7,8} and low social support^{9,10} on cognitive function or risk of dementia. The vast majority of these previous studies focused on social relations after retirement or in elderly people (age 65+), and only a few studies investigated social relations in midlife.^{11–14} However, factors in midlife such as negative aspects of close social relations,¹⁴ marital status,¹² and both political and mental activity¹³ have also been found to be associated with

cognitive function in old age. Thus, the adverse effect of poor social relations in private life on the risk of dementia is well established.

Recently, 17 studies on the relation of psychosocial working environment with cognitive function or risk of dementia were systematically reviewed and they revealed a gap in the literature on the relation between social relations at work and the risk of dementia.¹⁵ Likewise, from our literature search in PubMed and reading through the reference lists of relevant articles within the topic, we only found two (case-control) studies that have investigated the association between social relations at work and incident dementia.^{16,17} Andel et al¹⁶ found that low social support at work was associated with a higher risk of dementia, whereas Seidler et al¹⁷ reported that social climate at work and supervisor support were unrelated to dementia although the direction of the effect estimated indicated a higher risk of dementia among participants with a better social climate at work. Thus, the current empirical evidence of the influence of social relations *at work* on the risk of dementia is insufficient and conflicting.

Social relations at work are likely to affect cognitive health through the same mechanisms as have been suggested for social relations in private life. In general, lack of social interactions and insufficient social support are sources of stress.¹⁸ Thus, the suggested relationship between poor social relations and dementia may be due to a long-term activation of the physiological stress response.¹⁹ Stress increases the release of cortisol, which may cause hippocampal atrophy along with production and deposition of β -amyloid peptide (A β) in the brain.²⁰ Furthermore, social relations may influence health behaviors such as smoking, alcohol consumption, and physical activity,^{18,21} which may eventually influence cognitive health.

Knowledge about the effect of social relations at work on the risk of dementia would add to the understanding of the role of occupational exposures on dementia and would point the direction for future interventions. Therefore, we investigated whether social relations at work were associated with incident dementia in older age in a cohort of Danish employees comprising 1572 men who were followed for up to 29 years with an average of 15.8 years.

MATERIALS AND METHODS

Study Population

The study population was drawn from the fourth wave of The Copenhagen Male Study (CMS). This study was initiated in 1970 to 1971 as a prospective cohort study investigating cardiovascular risk factors. Initially, the study included 5249 Caucasian men from 14 different large workplaces in Copenhagen with a mean age of 48 years. The participants were reinvited in 1972, 1976, and 1985 for subsequent follow-ups.²² At the fourth wave carried out between June 1985 and June 1986, all 4505 participants (710 men had died and 34 men had emigrated) from the cohort were traced through the Danish Central Population Register and were invited to participate in the study. Among these, 3387 (75.2%) agreed to participate.

From the 1684 participants who were still active on the labor market at the time of the 4th wave in 1985, participants for the current study had to fulfil the following criteria: (a) neither emigrated, diagnosed with dementia, nor had died within 5 years after

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The authors declare no conflicts of interests.

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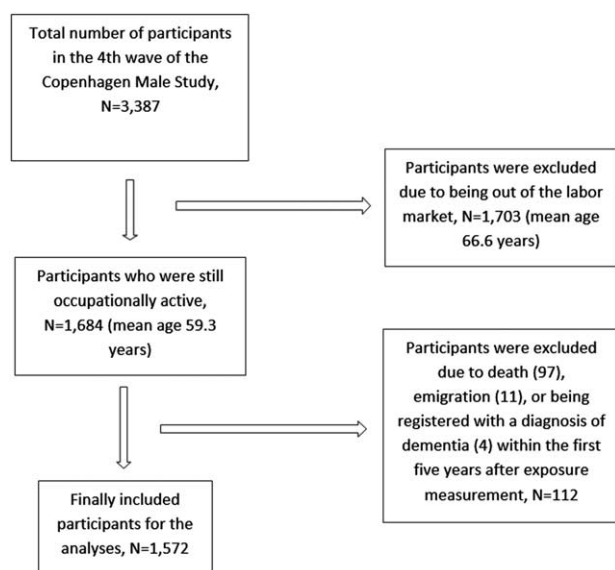


FIGURE 1. Selection of the study participants for the analyses.

participating in the data collection in order to reduce the risk of reverse causality and (b) survived to at least 60 years of age in order to ensure the validity of the dementia diagnosis, because the positive predictive value (PPV) for a dementia diagnosis is lower in young or middle-aged patients (PPV 60%)²³ than in older patients (PPV 86%).²⁴ Applying these criteria resulted in study sample of 1572 participants with a mean age of 59.3 years at baseline. Figure 1 shows the selection of the study participants (Fig. 1).

The included participants were followed up until the date of a dementia diagnosis, emigration, death, or the end of 2014, whichever came first. Person-years were counted from 5 years after the exposure measurement or from the time, the participants turned 60 years and to the end of follow-up. Figure 2 shows the follow-up and risk period in all conditions (Fig. 2).

Dementia Diagnoses

Information about dementia diagnoses was obtained from the Danish national registers including The Danish Psychiatric Central

Research Register, The Danish National Patient Register, and The Danish Register of Causes of Death. Dementia diagnoses were registered according to WHO International Classification of Disease (ICD) criteria—ICD-8 in 1970 to 1993 and ICD-10 in 1994 onwards. The following diagnostic codes were used as outcome in the current study: Alzheimer's disease (ICD-8: 290.09; ICD-10: F00.0–9, G30.0–9), vascular dementia (ICD-8: 293.09–19; ICD-10: F01.0–9), frontotemporal dementia (ICD-8: 290.11; ICD-10: F02.0), dementia with Lewy bodies (ICD-10: G31.8), and dementia without specification (ICD-8: 290.09–19; ICD-10: F03.9, G31.9). However, we did not differentiate between the dementia subtypes in the analyses as the validity of the subtypes has been shown to be poor.²⁴

Social Relations at Work

Quantitative aspects (ie, the structural aspects) of social relations²⁵ at work were measured by asking: (1) “Do you have the possibility to be in contact with coworkers during working hours?” Response options were (a) good possibilities, (b) some possibilities, (c) limited possibilities, and (d) I work alone.

Qualitative aspects (ie, the functional aspects) of social relations²⁵ at work were measured by two questions: (2) “Do you and your coworkers get along with each other?” Response options were (a) yes, absolutely, (b) yes, most of the time, (c) neither yes nor no, and (d) no, absolutely not; and (3) “How satisfied are you with your immediate supervisor?” Response options were (a) very satisfied, (b) fairly satisfied, (c) neither satisfied nor dissatisfied, (d) dissatisfied, and (e) very dissatisfied. In all analyses, the four original categories were used for question 1 while question 2 and 3 were dichotomized due to a low number of respondents in some of the response categories. As reference category we used response option “a” (good possibilities) for question 1, “a” and “b” (yes, absolutely/most of the time) for question 2 and “a,” “b,” and “c” (very/fairly satisfied/neither satisfied nor dissatisfied) for question 3.

Covariates

From the national registers, we obtained information about the participants' age, educational attainment (0 to 9 years, 11 to 12 years, greater than 12 years of formal schooling), cardiovascular disease (CVD) before baseline (ie, any ischaemic heart disease and cerebrovascular disease before baseline, yes/no), and any record of hospitalization in a psychiatric ward or hospital before baseline (yes/no).

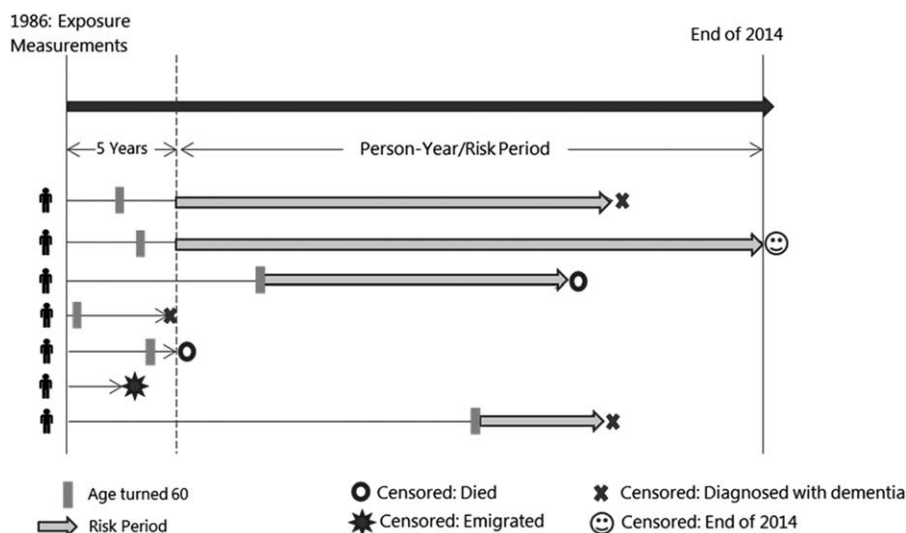


FIGURE 2. Participants' follow-up and underlying risk period.

From the questionnaire, we obtained self-reported information about marital status (either married/cohabiting or divorced/separated/widow/single), children living at home (yes/no), CVD risk factors (average alcohol consumption per weekdays and per weekend, smoking habits: never/past/current, leisure time physical activity: less than 2 hours/2 to 4 hours/greater than 4 hours), sleep problems (difficulties falling asleep at night, waking early morning without having had enough sleep), work-related factors (job control: high/some/very low or not at all, work pace: fast/appropriate/slow, and monotonous work: varied/neither varied nor monotonous/monotonous) was collected from survey data.

From clinical examination, we obtained information about body mass index (BMI = weight in kilogrammes divided by the squared height in meters) and systolic blood pressure (mmHg). Age, BMI, systolic blood pressure, and average alcohol consumption per week were analyzed as continuous variables.

In the analyses and interpretation of the findings, we included participants' educational attainment, marital status, children living at home, and work related factors as confounders in the association between social relations at work and incident dementia.^{15,26} Our measure of CVD is interpreted as a confounder as it is assessed before the assessment of the social relations at work. Finally, the CVD risk factors (average alcohol consumption per week, smoking habits, leisure time physical activity, BMI, and systolic blood pressure) and poor sleep which were assessed at the same time as the social relations at work may have the potential to play a role as both confounders²⁶ and mediators.^{26,27}

Statistical Analyses

We performed an exploratory analysis with chi-squared test for all categorical variables and *t* test for all continuous variables to examine whether the participants' characteristics differed according to their exposure status (Table 1).

Participants' follow-up time was subdivided into 1-year intervals along the calendar time scale. For each interval, we computed the current age, time since exposure measurement, and calendar year. Then, we estimated incident rate ratios (IRR) with 95% confidence interval (CI) from our analyses of the association between social relations at work and incident dementia in old age. All the IRRs were estimated by modelling the event of a dementia diagnosis as a function of the exposure in a Poisson regression model.²⁸

In order to adjust for potential confounding in multivariate analyses, we built three models by including a priori selected covariates in blocks (Table 1). In Model 1, we adjusted for current age in each calendar year, time since exposure measurement, calendar year, and all three measures of social relations at work. In Model 2, we additionally adjusted for potential confounders including marital status, children living at home, educational attainment, work-related factors including job control, work pace, and monotonous work. In Model 3, we further adjusted for CVD before baseline, CVD risk factors at baseline (average alcohol consumption per week, smoking habits, leisure time physical activity, BMI, and systolic blood pressure), and sleep problems. The latter group of covariates may potentially act as either confounders or mediators.

In the first additional analysis, we excluded 24 participants who had at least one record of hospitalization in a psychiatric ward or hospital before start of follow-up. In the second additional analysis, we excluded 68 participants who had registered with a CVD diagnosis before baseline. Furthermore, in a third additional analysis, we compared the IRR of dementia among participants who did not work alone (ie, who answered good possibilities, some possibilities, or poor possibilities) versus participants who reported to work alone. All statistical analyses were conducted in SAS version 9.2 (SAS Institute Inc, Cary, NC).

Ethics

The study was approved by the Danish Data Protection Agency and no further ethical approval is required regarding register-based research in Denmark. The data set was stored at Statistics Denmark and was available by remote online access in an anonymous form.

RESULTS

Study population characteristics and incidence of dementia during follow-up are presented in Table 1. We found no difference in age, BMI, follow-up years, systolic blood pressure, and mean consumption of alcohol per weekday according to the reported level of social relations at work. However, the participants who reported having limited possibilities of being in contact with coworkers had less job control than those with better possibilities of being in contact with coworkers. A total number of 68 (4.3%) CVD cases before baseline was recorded (the distribution is not presented in Table 1 because of the very few cases in the different exposure categories; presenting these data violates the rule of Statistics Denmark who has provided access to data).

During an average of 15.8 years of follow-up, 245 participants (15.6% of the study sample) were diagnosed with dementia. The percentage of incident dementia cases was higher among men who had limited possibilities to be in contact with coworkers (25%) compared with men who had good possibilities (14.6%) and men who did not get along with their coworkers (27.3%) compared with men who reported getting along with coworkers (15.3%) (Table 1).

The results of the univariate and multivariate analyses consistently showed that participants with limited possibilities to be in contact with coworkers during working hours had a higher rate of incident dementia compared with those with good possibilities (Table 2). The estimated IRRs were 2.49 (95% CI: 1.14 to 5.44) in model 2 when adjusting for potential sociodemographic and work-related confounders. The estimate did not change remarkably, when we adjusted for CVD before baseline and potential mediators (CVD risk factors and sleep). The IRR for dementia was also higher among men who reported to work alone compared with men who had good possibilities to be in contact with coworkers as the IRR was 1.17 (95% CI: 0.71 to 1.92) in model 2.

Compared with men who get along with their coworkers, the IRR of dementia was higher among men who reported that they did not get along with their coworkers as the IRR was 1.64 (95% CI: 0.76 to 3.54) in model 2. The estimate remained similar when CVD before baseline and the potential mediators were further adjusted for (Table 2). These estimates were not statistically significantly different from unity.

The association between the participants' level of satisfaction with their supervisor and incident dementia was also statistically insignificant in all models, although a lower IRR for dementia was observed among participants who reported dissatisfaction with their supervisors (IRR = 0.83; 95% CI: 0.60 to 1.15, model 2) (Table 2).

In an additional analysis, we included only participants without a record of hospitalization in a psychiatric ward or hospital. In this subsample, the results from model 2 showed consistent associations when compared with the main analyses with an IRR of 2.13 (95% CI: 0.95 to 4.78) of dementia in men who had limited possibilities versus men who had good possibilities of being in contact with coworkers (not shown in tables). The estimate for the same association stayed consistent with an IRR of 1.95 (95% CI: 0.76 to 4.97) in model 2 in the second additional analysis where participants with a CVD diagnosis before baseline were excluded (not shown in tables).

Furthermore, in an additional analysis, we investigated the risk of dementia in participants who reported to work alone versus who did not work alone (combining all other response groups in

TABLE 1. Incident Dementia During the Follow-Up and Baseline Characteristics of the Study Population of 1572 Men According to Exposure Status

Characteristics	Possibilities to be in Contact With Coworkers				P	Get Along With Coworkers		Satisfaction With Supervisor			
	Good, N = 1,174	Some, N = 274	Limited, N = 28	Work Alone, N = 96		Yes*, N = 1,539	No†, N = 33	Satisfied†, N = 1,210	Dissatisfied§, N = 362	P	
Outcome											
Dementia cases during follow-up, N (%)	171 (14.6)	45 (16.4)	7 (25.0)	22 (22.9)	0.08	236 (15.3)	9 (27.3)	0.06	192 (15.9)	53 (14.6)	0.57
Baseline characteristics¶											
Model 1											
Age (in yrs), mean (SD)	56.2 (3.5)	59.3 (3.6)	58.6 (2.9)	59.4 (3.8)		59.3 (3.6)	58.4 (2.6)	0.14	59.3 (3.6)	59.1 (3.4)	0.36
Follow-up (yrs), mean (SD)	15.5 (7.1)	16.4 (6.9)	12.8 (7.1)	16.2 (7.0)		15.7 (7.1)	16.8 (7.3)	0.35	15.7 (7.1)	15.6 (7.1)	0.80
Model 2											
Divorced/separated/widow/single, N (%)	109 (9.3)	24 (8.8)	Few obs. #	11 (11.5)	0.56	140 (9.1)	4 (12.1)	0.56	113 (9.4)	31 (8.6)	0.68
No children living at home, N (%)	960 (81.8)	235 (86.1)	Few obs. #	85 (88.5)	0.13	1,279 (83.1)	26 (78.8)	0.51	999 (82.6)	306 (84.5)	0.38
Educational attainment: ≤9 yrs, N (%)	435 (37.1)	109 (39.8)	10 (35.7)	34 (35.4)	<0.01	578 (37.6)	10 (30.3)	0.05	458 (37.9)	130 (35.9)	0.79
Low job control, N (%)	116 (10.0)	53 (19.3)	15 (53.6)	37 (39.0)	<0.01	214 (14.0)	7 (21.2)	0.43	143 (11.9)	78 (21.6)	<0.01
Have fast-paced work, N (%)	344 (29.7)	97 (36.1)	10 (37.0)	31 (32.6)	0.20	475 (31.3)	7 (21.2)	0.21	346 (29.0)	136 (38.4)	<0.01
Monotonous work, N (%)	161 (13.8)	68 (24.9)	6 (21.4)	22 (22.9)	<0.01	247 (16.1)	10 (30.3)	0.03	169 (14.1)	88 (24.4)	<0.01
Model 3											
Alcohol (mean number of units per weekday), mean (SD)	4.1 (1.0)	3.9 (1.0)	3.8 (0.9)	3.9 (1.0)		4.0 (1.0)	4.5 (1.2)	0.02	4.0 (1.0)	4.1 (1.1)	0.39
Current smoker, N (%)	633 (54.4)	142 (52.4)	14 (50.0)	52 (54.2)	0.96	822 (53.9)	19 (57.6)	0.50	667 (55.7)	174 (48.2)	0.03
Physical activity (Leisure time) <2hr, N (%)	132 (11.3)	34 (12.5)	Few obs. #	13 (13.8)	0.38	177 (11.6)	4 (12.1)	0.99	127 (10.5)	54 (15.0)	0.04
BMI (kg/m ²), mean (SD)	25.7 (3.3)	25.8 (3.1)	25.0 (3.2)	26.3 (4.0)		25.7 (3.3)	25.1 (2.9)	0.26	25.7 (3.3)	25.8 (3.3)	0.50
Systolic blood pressure (mmHg), mean (SD)	120 (17)	118 (16)	123 (15)	122 (17)		120 (17)	124 (14)	0.21	120 (17)	120 (16)	0.52
Have sleep problems, N (%)	247 (21.0)	76 (27.7)	8 (28.6)	20 (20.8)	0.09	342 (22.2)	9 (27.3)	0.49	249 (20.6)	102 (28.2)	<0.01

BMI, body mass index; SD, standard deviation.

*Yes, absolutely/yes, most of the time.

†Neither yes nor no/no, absolutely not.

‡Very satisfied/fairly satisfied.

§Neither satisfied nor dissatisfied/dissatisfied-Quite dissatisfied/very dissatisfied.

¶According to the order of the covariates adjusted in the multivariate models.

#Few obs.—due to a restriction from the Statistics Denmark, we were not allowed to present any information which contains a frequency ≤3.

TABLE 2. Incidence Rate ratios (IRR) With 95% Confidence Interval (CI) for Incident Dementia Among the Participants According to their Level of Social Relations at Work in the Copenhagen Male Study

Social Relations at Work	No. of Participants With Dementia <i>N</i> = 245	Univariate IRR (95% CI)	Multivariate		
			Model 1, IRR (95% CI)	Model 2, IRR (95% CI)	Model 3, IRR (95% CI)
Possibilities to be in contact with coworkers					
Good possibilities	171	1	1	1	1
Some possibilities	45	1.07 (0.79–1.49)	1.02 (0.73–1.42)	0.98 (0.69–1.38)	1.09 (0.77–1.54)
Limited possibilities	7	2.16 (1.11–4.20)	3.05 (1.44–6.50)	2.49 (1.14–5.44)	2.74 (1.23–6.11)
I work alone	22	1.50 (1.00–2.25)	1.39 (0.85–2.25)	1.17 (0.71–1.92)	1.25 (0.75–2.10)
Get along with coworkers					
Yes, absolutely/yes, most of the time	236	1	1	1	1
Neither yes nor no/no, absolutely not	9	1.81 (0.94–3.50)	1.54 (0.71–3.30)	1.64 (0.76–3.54)	1.52 (0.70–3.31)
Satisfaction with supervisor					
Very satisfied/fairly satisfied/	192	1	1	1	1
Neither satisfied nor dissatisfied/ dissatisfied/very dissatisfied	53	0.92 (0.69–1.24)	0.91 (0.67–1.25)	0.83 (0.60–1.15)	0.79 (0.57–1.10)

Model 1: Adjusted for current age in each calendar year, time since exposure measurement, calendar year and all three measures of social relations at work.

Model 2: Model 1+ participants' marital status, children living at home, educational attainment, work-related factors including job control, work pace, and monotonous work.

Model 3: Model 2+ CVD before baseline, CVD risk factors (average alcohol consumption per week, smoking habits, leisure time physical activity, BMI, and Systolic blood pressure), and sleep problems.

one) and the estimated IRR was not statistically significant (1.13, 95% CI: 0.69 to 1.84, model 2) (not shown in tables).

DISCUSSION

We investigated the association between three measures of social relations at work and the risk of incident dementia in a longitudinal study of 1572 Danish middle-aged male employees. Limited possibilities of being in contact with coworkers were associated with a higher risk of dementia in old age. However, social relations as indicated by the participants' ability to get along with coworkers and the level of satisfaction with supervisors were not statistically significantly associated with a higher risk of dementia.

Comparison With Previous Findings

In a case-control study based on Swedish twin data, lower social support at work was found to be associated with a higher risk of dementia with an odds ratio (OR) of 1.15 (95% CI: 1.03 to 1.28). In this study, social support at work was measured as possibilities for helpful social interaction and support from coworkers and supervisor.¹⁶ Our findings showed a higher risk of dementia among participants who reported limited possibilities of being in contact with coworkers. Limited possibilities to be in contact with coworkers were likely to reduce the possibility of experiencing social support from coworkers, which may partly explain the observed increased risk. Also, a German case-control study reported a potentially protective effect of supervisor support on the risk of dementia as high supervisor support was associated with an OR of 0.7 (95% CI: 0.4 to 1.4) for dementia.¹⁷ Supervisor support was assessed by five items related to encouragement, trust, and support from supervisor. In contrast, the same study found that better social climate was associated with higher risk of dementia (OR 1.3, 95% CI: 0.8 to 2.2), and the authors reported that the estimate became statistically significant when the analysis was restricted to cases without any CVD.¹⁷ Social climate at work was assessed by four items related to the degree of open communication, information flow, and cooperation.¹⁷

These previous studies of social relations at work and dementia have solely focused on qualitative aspects of social relations at work and have assessed social relations as composite measures

combining factors such as helpful social interactions and support at work.^{16,17} In our study, we included both qualitative and quantitative aspects of social relations at work and analyzed these aspects separately. A French study comparing qualitative and quantitative aspects of private life social relations on the risk of dementia in an older population found that the qualitative aspects of social relations were associated with the risk of dementia while this was not the case for quantitative aspects of social relations.²⁹ In contrast, we found that quantitative aspects of social relations at work such as limited possibilities of being in contact with coworkers were associated with a higher risk of dementia, whereas qualitative aspects of social relations at work such as satisfaction with supervisors or getting along with coworkers did not seem to be associated with the risk of dementia.

Contrary to our expectation, we did not find that participants who reported to work alone had a higher risk of dementia in old age. It is possible that individuals who work alone have deliberately chosen a job without any colleagues. However, in the additional analysis, working alone was not found to be associated with the risk of dementia compared with all other participants who did not work alone. Therefore, it seems that working alone may not be as detrimental as having coworkers but not being able to be in contact with these coworkers. Nevertheless, it may also indicate that possibilities to be in contact with coworkers may not reflect an effect of social relations at work.

Discrepancies between the two previous studies^{16,17} and the present study may partly be due to different measures of social relations. In the current study we used self-reported information on social relations at work, assessed only once for the participants' midlife or late midlife job. The two previous studies linked participants' job title with a job-exposure matrix to assess the level of exposure either for the main lifetime occupation only¹⁶ or all lifetime occupations.¹⁷

Strengths and Limitations

The main strength of the current study was the long follow-up time and the exclusion of participants with dementia diagnosis within the first 5 years after the assessment of social relations to reduce the risk of reverse causation. Still, the long follow-up time may also have diluted the effect of social relations on the risk of

dementia. This potential dilution appears unavoidable when investigating long-term effects of midlife exposures on outcomes, such as dementia, occurring in old age. Other strengths include the use of objectively measured (ie, not self-reported) dementia diagnoses as the outcome. Outcome information was retrieved from three national registers covering all deaths, psychiatric and somatic inpatient contacts and from 1995 onwards also all outpatient and emergency room contacts. In contrast to previous studies,^{16,17} we adjusted for a wide range of covariates, registered at the time of exposure measurement, including socio-demographic factors, CVD before baseline, CVD risk factors, sleep problems, and work-related factors.

One of the main limitations of the study was that the participants' social relations at work were measured at only one point in time and that the measures of social relations reflected only a few aspects of social relations at work.²⁵ Thus, exposure misclassification could be an issue that might have influenced our results and diluted the observed associations. The importance of workplace social relations and related concepts was not generally acknowledged until later, for example, with the introduction of social support into the job-strain model.³⁰ Current studies on occupational risk factors in midlife and dementia in old age were therefore depending on the data collection occurring decades ago, and not until the 1990s and 2000s validated scales assessing social relations at work (eg, social support and social capital) became part of questionnaires aiming at making broad evaluations of the psychosocial working environment.

Other job characteristics such as job control and job complexity may confound the association between social relations at work and dementia. In the current study low job control, fast-paced work and monotonous work were differentially distributed between groups with good and limited possibilities to be in contact with their coworkers. Previous studies have found that low job control may be a risk factor for dementia,¹⁵ but in our study, the association between social relations and dementia did not change substantially when adjusting for job control. We did not have information on job complexity, but a previous study found that adjusting for job complexity strengthened the association between social support at work and the risk of dementia.¹⁶ Still, adjustment for work pace, monotonous work, and educational attainment did not substantially change the observed associations.

Among the unmeasured potential confounders are private life social relations which have been widely reported to influence the risk of dementia.¹ In the current study, we adjusted for marital status and children living at home, which reflect aspects of private life social relations. Perhaps a more important unmeasured factor is cognitive ability since cognitive ability is likely to influence selection into different types of jobs.³¹ To the extent that individual's occupation/jobs differ by both cognitive ability and social relations at work, associations between social relations and risk of dementia may reflect associations between cognitive ability earlier in life and the later life risk of dementia. Educational attainment tends to be strongly correlated with cognitive ability in both young adulthood and later life.³² Nevertheless, in this study, educational attainment was not associated with the risk of dementia, and this suggests that confounding by cognitive ability may not have had a major impact on the results or that our measure of educational attainment in this cohort born between 1912 and 1932 did not adequately reflect cognitive ability.

The validity of the registered dementia diagnoses may also have influenced our results. A recent study found that nearly 86% of the registered diagnoses of dementia in Denmark matched the report of the corresponding medical journal,²⁴ but it has also been reported that the hospital registers only capture about two-thirds of all cases in Denmark.³³ Unregistered cases may have diluted the observed associations. Perhaps more important, the development from early

subclinical changes to clinically manifested dementia may last from a few years to decades.³⁴ Thus, early stages of dementia may influence the perception of social relations at work or result in selection into job types with little contact with coworkers. Bias due to this type of reporting bias will be substantial if the prevalence of very early subclinical symptoms is high and strongly associated with social relations at work.

"Genetic factors and family history of dementia may have influenced our results. For example, the Apolipoprotein E (ApoE) $\epsilon 4$ allele is considered to be one of the major risk factors for dementia in old age,²⁶ and ApoE $\epsilon 4$ carriers appear to be more susceptible than non-carriers to the effect of negative life events (such as death of a spouse, loss of loved one, serious illness of a friend or relative, or a divorce) on cognitive impairment.³⁵ A previous study has shown that 17.4% of 41-year-old Danish men are ApoE $\epsilon 4$ carriers, and this proportion declines in older age groups.³⁶ If ApoE $\epsilon 4$ carriers are more susceptible to the effect of psychosocial stressors, it is plausible that the participants in our study, who reported to have limited possibilities to be in contact with coworkers, have a higher risk of developing dementia if they carry the ApoE $\epsilon 4$ allele. If so, in our results the risk is likely to be underestimated for ApoE $\epsilon 4$ carriers and overestimated for non-carriers. However, we cannot support this hypothesis with empirical data, as we did not know whether the participants were ApoE $\epsilon 4$ carriers. Neither did we have questionnaire data about the participants' family history of dementia, and the used cohort was too old to obtain this information from the Danish registers, as the national patient register is available in Denmark only from 1977 onwards."

Another concern is that we only included the 1572 occupationally active participants out of the 3387 participants in the 4th survey of the CMS, which may lead to some degree of healthy worker selection bias. However, the mean age of the excluded men was 66.6 years at the time of exposure measurement, indicating that retirement due to old age was probably the main factor driving this selection. The percentages of dementia, among the excluded and the included men were comparable being 14.3% and 15.6% and unadjusted incidence rates were 96 and 75 per 10,000 person-years, respectively. Hence, healthy worker selection seems unlikely to have influenced our results substantially.

Finally, our findings of a higher risk of dementia in the participants with limited possibilities to be in contact with coworkers were based on only seven dementia cases in the exposed group. An estimate based on few cases can be vulnerable to even a small variation in the number of cases. Thus, the observed association in our study could be a chance finding. However, our result is in accordance with the literature on social relations and dementia.¹

It would also be worthwhile to know the role of social relations at work on the subtypes of dementia, for example, Alzheimer's disease, vascular dementia, frontotemporal dementia, dementia with Lewy bodies. However, due to a poor diagnostic validity of subtypes of dementia in the Danish registers and a lack of sufficient power,²⁴ in the current study, we were not able to investigate the association between social relations at work and incident dementia for subtypes of dementia.

CONCLUSION

This is the first prospective study to investigate the effect of social relations at work on the risk of dementia in old age. In conclusion, our data partially support the hypothesis of an effect of social relations at work on incident dementia in old age, as we found that men who reported limited possibilities to be in contact with coworkers were at higher risk of developing dementia in old age. The present study could not confirm that measures of qualitative aspects of social relations at work, such as getting along with coworkers and satisfaction with supervisor were related to the risk of dementia.

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